

SEQUENCE LISTING

D) >
<110> WALLACH, David
GOLTSEV, Yura
KOVALENKO, Andrei
VARFOLOMEEV, Eugene
BRODIANSKI, Vadim

<120> CASH (CASPASE HOMOLOGUE) WITH DEATH EFFECTOR DOMAIN,
MODULATORS OF THE FUNCTION OF FAS RECEPTORS

<130> WALLACH=23

<140> 09/380,546
<141> 1999-11-29

<150> PCT/IL98/00098
<151> 1998-02-26

<150> IL 120367
<151> 1997-03-03

<150> IL120759
<151> 1997-05-01

<160> 20

<170> PatentIn Ver. 2.0

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Met Ser Ala Glu Val Ile His Gln Val Glu Glu Ala Leu Asp Thr Asp

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His Ser Ser Pro Ser Leu Tyr Leu Gln Cys Leu Ser Gln Lys Leu Arg		
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Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
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Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu
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Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln
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Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys
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Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Leu His Asn Gly Arg Ser
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Lys Lys Ser Ile Gln Glu Ser Glu Ala Phe Leu Pro Gln Ser Ile Pro
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Glu Glu Arg Tyr Lys Met Lys Ser Lys Pro Leu Gly Ile Cys Leu Ile
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His Ser Ser Pro Ser Leu Tyr Leu Gln Cys Leu Ser Gln Lys Leu Arg
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Gln Glu Arg Lys Arg Pro Leu Leu Asp Leu His Ile Glu Leu Asn Gly
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 Met Ser Ala Glu Val Ile His Gln Val Glu Ala Leu Asp Thr Asp
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 Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg
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 Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
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 Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu
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 atg gca gag att ggt gag gat ttg gat aaa tct gat gtg tcc tca tta 817
 Met Ala Glu Ile Gly Glu Asp Leu Asp Lys Ser Asp Val Ser Ser Leu
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Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln		
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Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys		
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Ser Leu Lys Asp Pro Ser Asn Asn Phe Arg Met Ile Thr Pro Tyr Ala		
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His Cys Pro Asp Leu Lys Ile Leu Gly Asn Cys Ser Met		
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Val Pro Pro Asn Val Arg Asp Leu Leu Asp Ile Leu Arg Glu Arg Gly		
35	40	45
Lys Leu Ser Val Gly Asp Leu Ala Glu Leu Leu Tyr Arg Val Arg Arg		
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Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu		
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Thr His Leu Leu Arg Asn Pro His Leu Val Ser Asp Tyr Arg Val Leu		
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Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu
 115 120 125

Lys Ser Phe Leu Asp Leu Val Val Glu Leu Glu Lys Leu Asn Leu Val
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Ala Pro Asp Gln Leu Asp Leu Leu Glu Lys Cys Leu Lys Asn Ile His
 145 150 155 160

Arg Ile Asp Leu Lys Thr Lys Ile Gln Lys Tyr Lys Gln Ser Val Gln
 165 170 175

Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys
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His Cys Pro Asp Leu Lys Ile Leu Gly Asn Cys Ser Met
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Leu Ser Glu Arg Gly Gln Leu Ser Phe Ala Thr Leu Ala Glu Leu Leu
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Tyr Arg Val Arg Arg Phe Asp Leu Leu Lys Arg Ile Leu Lys Thr Asp
 65 70 75 80

Lys Ala Thr Val Glu Asp His Leu Arg Arg Asn Pro His Leu Val Ser
 85 90 95

Asp Tyr Arg Val Leu Leu Met Glu Ile Gly Glu Ser Leu Asp Gln Asn
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Asp Val Ser Ser Leu Val Phe Leu Thr Arg Ile Thr Arg Asp Tyr Thr
 115 120 125

Gly Arg Gly Lys Ile Ala Lys Asp Lys Ser Phe Leu Asp Leu Val Ile
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Glu Leu Glu Lys Leu Asn Leu Ile Ala Ser Asp Gln Leu Asn Leu Leu
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Glu Lys Cys Leu Lys Asn Ile His Arg Ile Asp Leu Asn Thr Lys Ile
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Gln Lys Tyr Thr Gln Ser Ser Gln Gly Ala Arg Ser Asn Met Asn Thr
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Leu Gln Ala Ser Leu Pro Lys Leu Ser Ile Lys Tyr Asn Ser Arg Leu
 195 200 205

Gln Asn Gly Arg Ser Lys Glu Pro Arg Phe Val Glu Tyr Arg Asp Ser
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Gln Arg Thr Leu Val Lys Thr Ser Ile Gln Glu Ser Gly Ala Phe Leu
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Pro Pro His Ile Arg Glu Glu Thr Tyr Arg Met Gln Ser Lys Pro Leu
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Gln Glu Thr Phe Thr Ser Leu Gly Tyr His Ile Gln Leu Phe Leu Phe
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Pro Lys Ser His Asp Ile Thr Gln Ile Val Arg Arg Tyr Ala Ser Met
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Ala Gln His Gln Asp Tyr Asp Ser Phe Ala Cys Val Leu Val Ser Leu
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Gly Gly Ser Gln Ser Met Met Gly Arg Asp Gln Val His Ser Gly Phe
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Ser Leu Asp His Val Lys Asn Met Phe Thr Gly Asp Thr Cys Pro Ser
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Leu Arg Gly Lys Pro Lys Leu Phe Phe Ile Gln Asn Tyr Glu Ser Leu
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Gly Ser Gln Leu Glu Asp Ser Ser Leu Glu Val Asp Gly Pro Ser Ile
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Lys Asn Val Asp Ser Lys Pro Leu Gln Pro Arg His Cys Thr Thr His
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Pro Glu Ala Asp Ile Phe Trp Ser Leu Cys Thr Ala Asp Val Ser His
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Leu Glu Lys Pro Ser Ser Ser Val Tyr Leu Gln Lys Leu Ser
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Gln Gln Leu Lys Gln Gly Arg Arg Pro Leu Val Asp Leu His Val
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Gln Glu Lys Arg Met Leu Glu Glu Ser Asn Leu Ser Phe Leu Lys Glu
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Leu Leu Phe Arg Ile Asn Arg Leu Asp Leu Leu Ile Thr Tyr Leu Asn
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Ser Lys Cys Lys Leu Asp Asp Asp Met Asn Leu Leu Asp Ile Phe Ile
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Glu Met Glu Lys Arg Val Ile Leu Gly Glu Gly Lys Leu Asp Ile Leu
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Lys Arg Val Cys Ala Gln Ile Asn Lys Ser Leu Leu Lys Ile Ile Asn
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Asp Tyr Glu Glu Phe Ser Lys Glu Arg Ser Ser Ser Leu Glu Gly Ser
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Pro Asp Glu Phe Ser Asn Gly Glu Glu Leu Cys Gly Val Met Thr Ile
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Ser Asp Ser Pro Arg Glu Gln Asp Ser Glu Ser Gln Thr Leu Asp Lys
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Val Tyr Gln Met Lys Ser Lys Pro Arg Gly Tyr Cys Leu Ile Ile Asn
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 Asn His Asn Phe Ala Lys Ala Arg Glu Lys Val Pro Lys Leu His Ser
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 Ile Arg Asp Arg Asn Gly Thr His Leu Asp Ala Gly Ala Leu Thr Thr
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 Thr Phe Glu Glu Leu His Phe Glu Ile Lys Pro His Asp Asp Cys Thr
 275 280 285
 Val Glu Gln Ile Tyr Glu Ile Leu Lys Ile Tyr Gln Leu Met Asp His
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 Ser Asn Met Asp Cys Phe Ile Cys Cys Ile Leu Ser His Gly Asp Lys
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 Lys Val Phe Phe Ile Gln Ala Cys Gln Gly Asp Asn Tyr Gln Lys Gly
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 Glu Gly Thr Trp Tyr Ile Gln Ser Leu Cys Gln Ser Leu Arg Glu Arg
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 Cys Pro Arg Gly Asp Asp Ile Leu Thr Ile Leu Thr Glu Val Asn Tyr
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Ile Glu Ala Asp Ala Leu Asn Pro Glu Gln Ala Pro Thr Ser Leu Gln
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Asp Ser Ile Pro Ala Glu Ala Asp Phe Leu Leu Gly Leu Ala Thr Val
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Pro Gly Tyr Val Ser Phe Arg His Val Glu Glu Gly Ser Trp Tyr Ile
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Gln Ser Leu Cys Asn His Leu Lys Lys Leu Val Pro Arg His Glu Asp
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Thr Phe Arg Asn Leu Lys Tyr Glu Val Arg Asn Lys Asn Asp Leu Thr
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Arg Glu Glu Ile Val Glu Leu Met Arg Asp Val Ser Lys Glu Asp His
 65 70 75 80

Ser Lys Arg Ser Ser Phe Val Cys Val Leu Leu Ser His Gly Glu Glu
 85 90 95

Gly Ile Ile Phe Gly Thr Asn Gly Pro Val Asp Leu Lys Lys Ile Thr
 100 105 110

Asn Phe Phe Arg Gly Asp Arg Cys Arg Ser Leu Thr Gly Lys Pro Lys
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 Glu Thr Asp Ser Gly Val Asp Asp Asp Met Ala Cys His Lys Ile Pro
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 Val Asp Ala Asp Phe Leu Tyr Ala Tyr Ser Thr Ala Pro Gly Tyr Tyr
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 Ser Trp Arg Asn Ser Lys Asp Gly Ser Trp Phe Ile Gln Ser Leu Cys
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 Ala Met Leu Lys Gln Tyr Ala Asp Lys Leu Glu Phe Met His Ile Leu
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 Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu Val
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 Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser Val
 85 90 95
 Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu Glu
 100 105 110
 Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe Leu
 115 120 125

Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys Lys His
 130 135 140
 Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe Asn Met
 145 150 155 160
 Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys Val Ile
 165 170 175
 Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp Phe Lys
 180 185 190
 Asp Ser Val Gly Val Ser Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu
 195 200 205
 Phe Glu Asp Asp Ala Ile Lys Lys Ala His Ile Glu Lys Asp Phe Ile
 210 215 220
 Ala Phe Cys Ser Ser Thr Pro Asp Asn Val Ser Trp Arg His Pro Thr
 225 230 235 240
 Met Gly Ser Val Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr
 245 250 255
 Ala Cys Ser Cys Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser
 260 265 270
 Phe Glu Gln Pro Asp Gly Arg Ala Gln Met Pro Thr Thr Glu Arg Val
 275 280 285
 Thr Leu Thr Arg Cys Phe Tyr Leu Phe Pro Gly His
 290 295 300

<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:fluorogenic substrate

<220>

<223> Asp at position 1 is modified with an acetyl group; Asp at position 4 is modified with an α-(4-methyl-coumaryl-7-amide) group

<400> 10

Asp Glu Val Asp
1

<210> 11

<211> 4

<212> PRT

<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<220>
<223> Tyr at position 1 is modified with an acetyl
group; Asp at position 4 may be modified with a
CH₂OOC(O)-[2,6(CF₃)₂] Ph group or an
a-(4-methyl-coumaryl-7-amide) group.

<400> 11
Tyr Val Ala Asp
1

<210> 12
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer
<400> 12
gactcgagtc tagagtcgac tttttttt tttttt

37

<210> 13
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer
<400> 13
aagttagcag atcagaattt ag

22

<210> 14
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer
<400> 14
gactcgagtc tagagtcgac

20

<210> 15
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 15
gaggatcccc aaatgcaaac tggatgatga c 31

<210> 16
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 16
gccaccagct aaaaacattc tcaa 24

<210> 17
<211> 31
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 17
ttggatccag atggacttca gcagaaatct t 31

<210> 18
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 18
attctcaaac cctgcattca agtg 24

<210> 19
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 19
ggcttctcggttcccaga gc 22

<210> 20
<211> 21
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 20

tgctcttcct gtgttagat g

21